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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,393	07/10/2001	Keith D. Allen	R-387	9468

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EXAMINER

TON, THAIAN N

ART UNIT PAPER NUMBER

1632

DATE MAILED: 06/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

09/903,393

Applicant(s)

ALLEN, KEITH D.

Examiner

Thaian N. Ton

Art Unit

1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 19 May 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on 19 May 2005. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 36-48.

Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____.
13. ☐ Other: _____.

For Waiver
AV1637

1. The Driscoll Declaration and Burke Declarations (filed 5/19/05) have been considered but are not persuasive and do not overcome the rejections of record. The Driscoll Declaration is directed to GAL1R knockout mice, which are not the mice of the instant invention, which are transgenic mice containing limulus clotting factor protease-like gene disruptions. The Burke declaration points to Deltagen's internal web-based Deltabase, representing a printout that discusses various changes relating to genotype associated with Gene 387. The declaration is not persuasive because it provides no nexus between "Gene 387" and limulus clotting factor protease-like gene, which is the subject of the instant invention. The declaration points to the top of the page for the nexus, but the top of this printout merely states that the name of the gene is an "unknown protease", and that its family is "protease" and subfamily is "serine protease". There is no particular indication that Gene 387 is limulus clotting factor protease-like gene. Furthermore, the Accession number GI number at the top of the print out are different from those presented in the specification. See p. 2, lines 23-24. Thus, given no nexus, different identification numbers, the information provided by the Burke declaration fail to overcome any of the prior rejections of record.

Continuation of 11. does NOT place the application in condition for allowance because: Applicants' argue that their amendments have now overcome the rejections of record. Briefly, Applicants argue that the 101 rejection, for utility, is satisfied by the instant invention. Particularly, that the protease-like +/- mouse would be used to study the function of the protease-like gene, and its association with, for example, pain and seizure, is specific to this mouse. See p. 8 of the Response. Applicants further argue that use of the mouse is substantial because it has a "real world use" as demonstrated by delivery of the claimed invention to at least one large pharmaceutical company, and provide evidence of commercial sale (through the Burke Declaration). See p. 10 of the Response. Applicants provide various arguments with regard to the fact that the instant case can be applied to the Brana case (see p. 12 of the Response); and that it is well-known for those of skill in the art that knockout mice are useful for studying gene function, the use of which, those of skill in the art would recognize as credible, substantial, and specific. See p. 14 of the Response. These arguments are not found to be persuasive for reasons of record advanced in the prior Office action (mailed 1/24/05). Namely, the knockout mice of the instant invention do not have substantial utility because, although it was scientifically well-known to knockout a gene to determine its function, this is not considered a substantial utility, because these knockout mice would be used for further research in the art, which is not considered a well-established utility. With regard to a "real-world use", the Burke Declaration (which has been addressed above) is not persuasive to provide guidance with regard to the commercial sale of the instantly claimed knockout mice. The asserted utility of the mice (for example, identifying agents that affect their phenotypes) is not readily apparent, because the teachings of record fail to provide a nexus between the limulus-clotting factor protease-like allele, and for example, a particular disease or disorder associated with it. Thus, this establishes that the contemplated utilities for these mice are neither specific nor substantial. It is reiterated that the instant case is not analogous to Brana, because the specification enabled the use. However, the mice of the instant invention do not exhibit a phenotype that correlates with the function of limulus clotting factor protease-like allele, and thus, the mice fail to have utility. Finally, it is reiterated that utilizing a particular visible marker, such as lacZ, is a general utility that can be used with any mouse knockout. The prior rejection under 101, is maintained for reasons of record.

The prior rejection of claims 36-48, under 112, 1st paragraph, is maintained for reasons of record advanced in the prior Office action (mailed 5/19/05). Applicants' remarks have been considered but are not persuasive. With regard to the comparing the instantly claimed mice with wild-type control mice, Applicants argue that it was well-known in the art to compare mice with controls of the same background, and provide the Burke declaration to show that the control mice were of identical background. The Burke declaration as evidence for this. The Burke declaration has been considered, but not found to be persuasive (see above). Applicants argue that the specification does not teach how to make a null allele; that the resulting phenotype is unpredictable; and that gene disruptions can lead to hypomorphic and hypermorphic alleles. Applicants argue that it is a general rule that disruption of a coding sequence by a positive selection marker, as taught by the specification, will result in a null allele; and that the Examiner has not presented any evidence supporting the position that the claimed mouse, having a null protease-like allele, was not made. See pp. 15-16 of the Response. The Examiner responds that there is no suggestion in the prior Office action that the claimed mouse was not made; it is that the art of producing knockout mice, in itself is unpredictable; thus, the resulting phenotype of these mice is unpredictable. Furthermore, all of the art provided in the prior Office actions do not suggest that a mouse of a "null protease-like allele" (the claims have now been amended to recite "limulus clotting factor protease-like allele") was not made, but that when producing transgenic knockout mice, various inbred strains react differently to the hot plate test, which, in turn, adds to the unpredictability found in the knockout art, when considering the resulting phenotype. Applicants argue that with regard to predictability, enablement is evaluated with respect to the claimed invention; the claim encompasses both heterozygous and homozygous mice. The heterozygous mice are useful for breeding homozygous mice and for phenotypic evaluation; and that any of the phenotypes associated with either +/- of -/- mice are inherent to the mice. Applicants further argue that ablation of function would be expected to result in the same phenotypic response; and thus, the Examiner has not provided any assertion that the mice of the instant invention, produced by the methods disclosed, would not predictably lead to a consistent phenotype. See pp. 16-17 of the Response. This is not persuasive for reasons of record; the plethora of art cited in previous Office actions provide ample guidance with regard to the art-recognized unpredictability of the knockout of a particular gene of interest, and that of the resulting phenotype. Even art provided by Applicants show this unpredictability (see Bilkie-Gorzo, and p. 16 of the Office action mailed 1/24/05). Furthermore, the specification only teaches the phenotypes of homozygous mice. Although one of skill would be able to make the heterozygous knockout mice, they have no particular phenotype. Thus, any of the uses contemplated by the specification would not be enabled with regard to the +/- mice.

The prior rejection of claims 36-48 under 112, 1st paragraph for written description (as a new matter rejection) is withdrawn in view of Applicants' cancellation of the term "null protease-like allele". The prior rejection of claims 36-48, under 112, 2nd paragraph, are withdrawn in view of Applicants' amendments.